Women with an ICD

Dr. Mirela Habibović

Affiliations

CoRPS
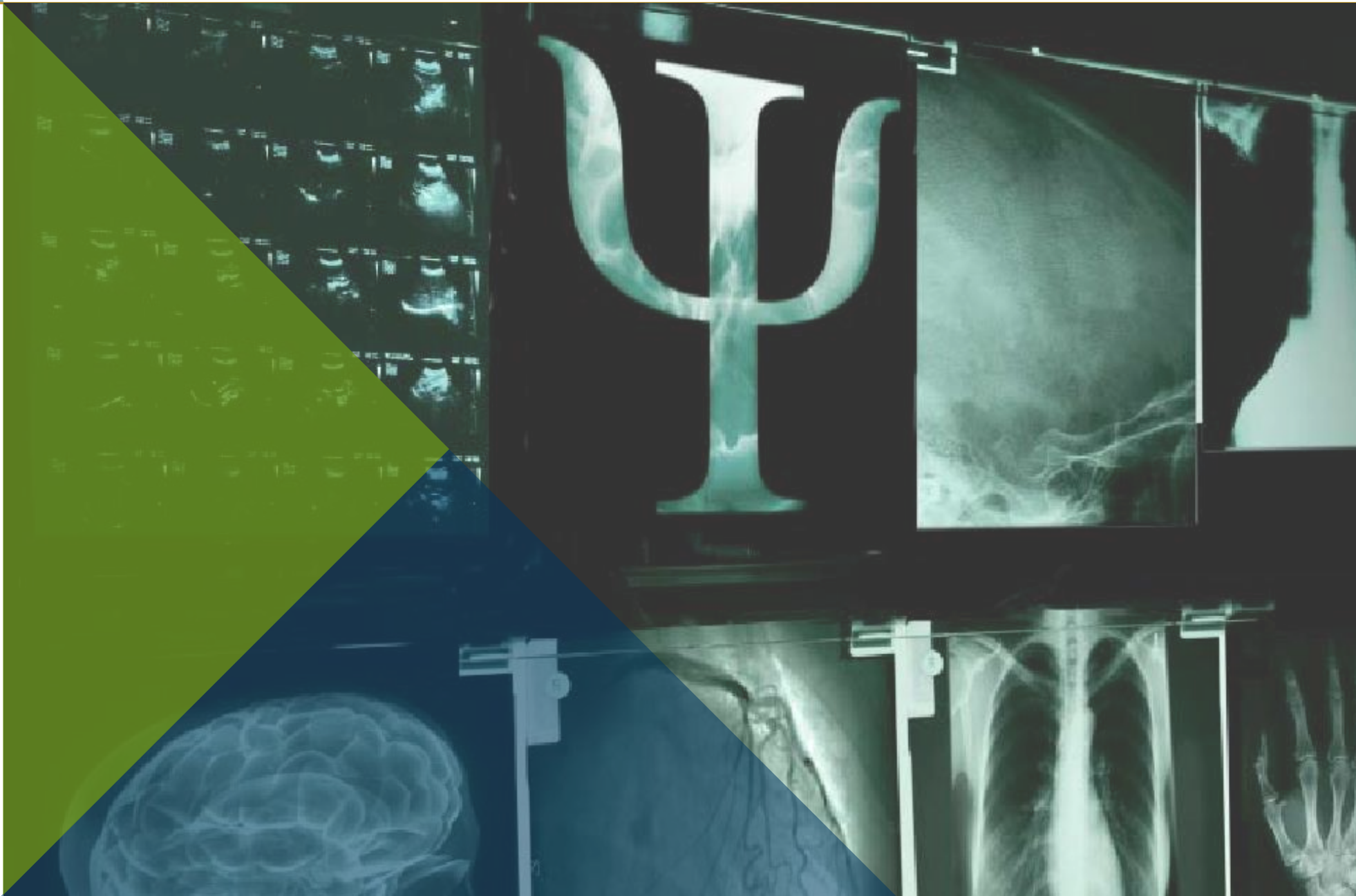
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Background

- **Increasing number of patients with an ICD worldwide**

- **33% of all ICD recipients are women**

- **Evidence that epidemiology and pathophysiology of cardiovascular disease differ in women and men**

- **Some suggestion that women and men may also differ in their arrhythmia susceptibility**

Haigney et al. Heart Rhythm 2009;6:180-6
Lampert et al. JACC 2004;43:2293-9

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- **A <u>paucity of studies</u> examined whether women are:**

  - **equally likely to be <u>implanted with an ICD</u> as men**

  - **experience the same level of <u>distress</u>, <u>body image concerns</u> and <u>quality of life</u> as men**

  - **more likely to experience <u>complications</u> than men**

  - **derive the same <u>health benefits</u> (i.e., survival) from ICD therapy as men**

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Gender and device-related complications

N=2954

Table 5. Rates of Device-Related Complications by Sex

| Device Type	Total (n=2882)	Women (n=754)	Men (n=2128)	P Value
All devices	241 (8.36%)	81 (10.74%)	160 (7.52%)	0.006
Single lead	43 (4.63%)	15 (6.91%)	28 (3.93%)	0.07
Dual lead	87 (8.34%)	23 (10.00%)	64 (7.87%)	0.30
CRT-D	111 (12.20%)	43 (14.01%)	68 (11.28%)	0.23

CRT-D indicates cardiac resynchronization therapy with defibrillator.

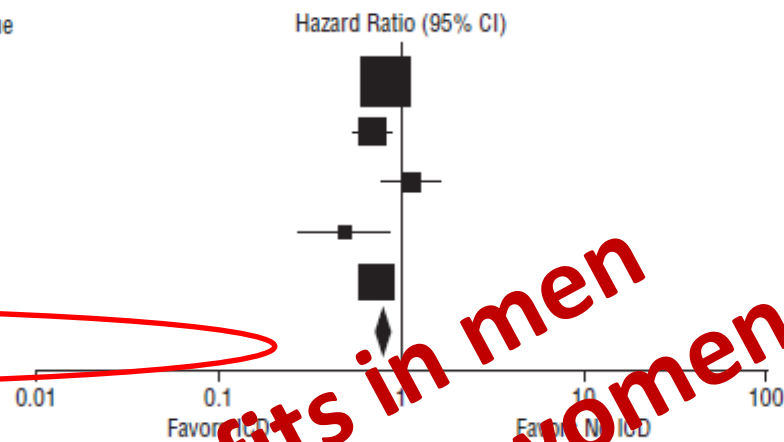# Gender disparities – procedure- and device-related complications

N =161,470

Peterson et al. Circulation 2009;119:1078-84

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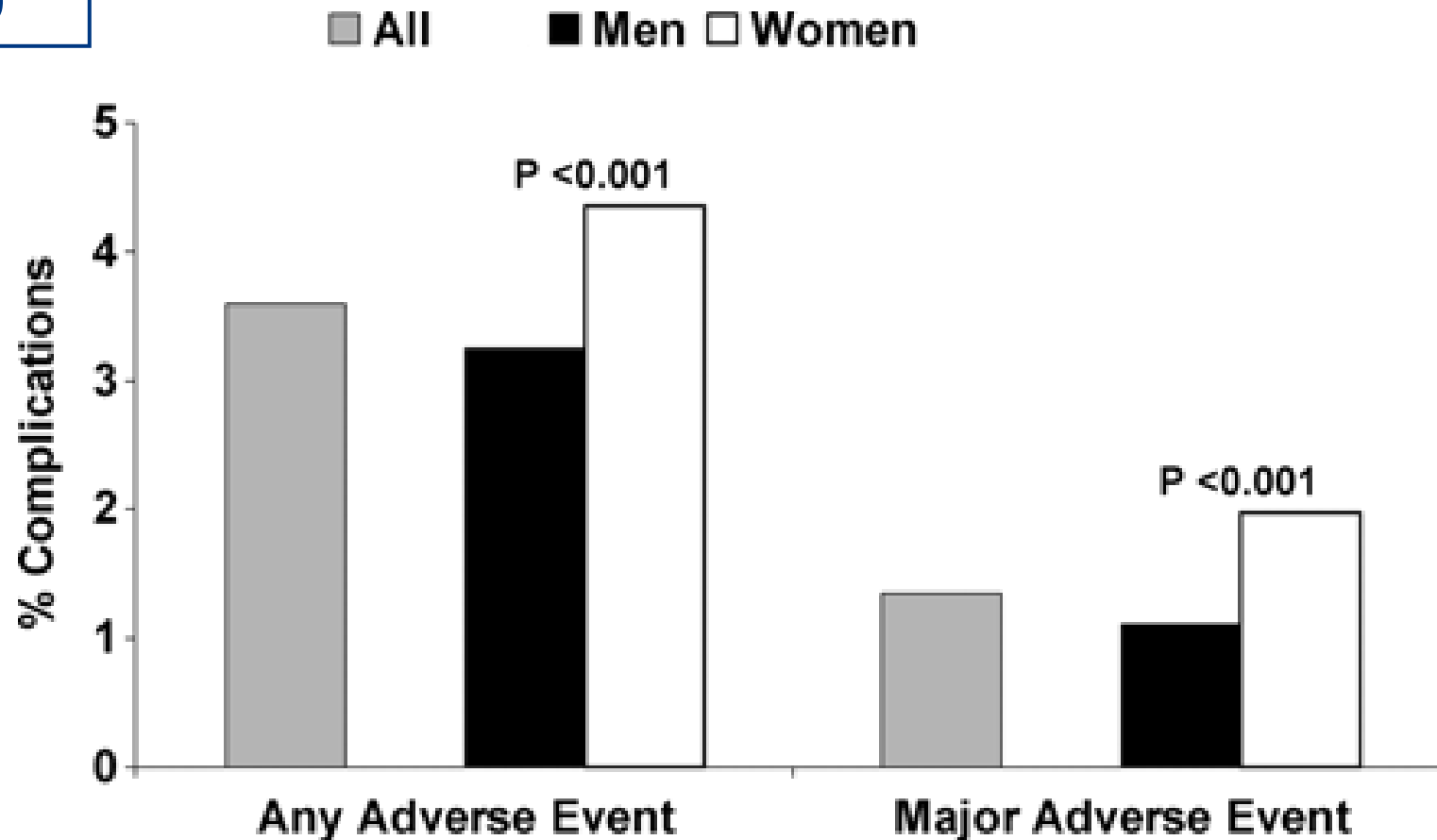
Gender differences - survival benefits ICD versus antiarrhythmics (meta-analysis - 1)
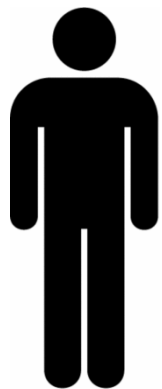
Study Name	Hazard Ratio	(95% CI)	No. of Men	P Value
MUSTT	0.83	(0.71-0.97)	636	.02
MADIT II	0.66	(0.48-0.91)	1040	.008
DINAMIT	1.14	(0.77-1.69)	514	.51
DEFINITE	0.49	(0.27-0.89)	326	.02
SCD-HeFT	0.71	(0.57-0.88)	1294	.004
Combined	**0.78**	**(0.70-0.87)**	**3810**	**<.001**

Study Name	Hazard Ratio	(95% CI)	No. of Women	P Value
MUSTT	1.64	(0.92-2.92)	68	.09
MADIT II	0.57	(0.28-1.18)	192	.12
DINAMIT	1.00	(0.49-2.04)	160	>.99
DEFINITE	1.14	(0.50-2.64)	132	.76
SCD-HeFT	0.90	(0.56-1.43)	382	.66
Combined	**1.01**	**(0.76-1.33)**	**934**	**.95**

Benefits in men but not in women

Ghanbari et al. Arch Intern Med 2009;169:1500-6

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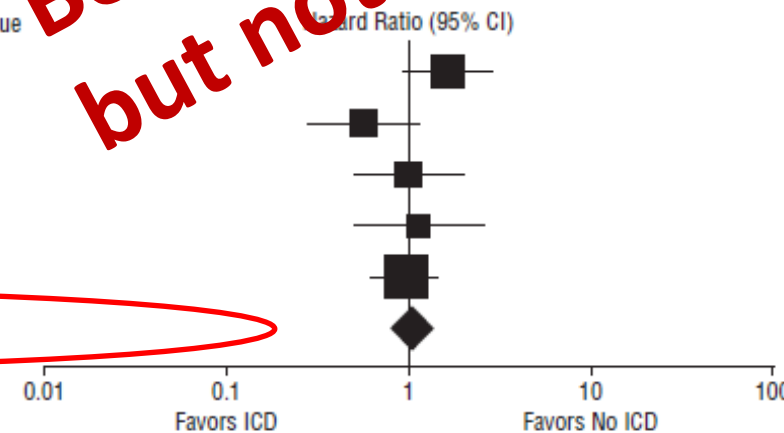
Patient Reported Outcomes

Men vs Women

Women	Men
Sensitivity of breast tissue	*No breast tissue*
Somato sensory amplification	*Lower awareness / attention body sensations*
Higher body awareness	*Lower body awareness*
Coping (social support)	*Fight or flight*
Socialy acceptable	*Less acceptable*

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FEMALE-ICD study (1)

Part 4: Being a Woman
- Family relationships
    How does ICD implantation affect your role as a wife, mother, daughter, etc.?
    How has your cardiovascular disease affected your family members?
    What can women do to enhance their role functioning?
- Changes in your body
    What are practical limitations of ICD implantation for women?
    How have changes in your body after implantation affected your body image?
    What are strategies for developing better body image and increasing confidence?
- Romantic relationships, sex, and intimacy
    Have you experienced changes in romantic relationships after ICD implantation?
    Do you have fears regarding sexual activity?
    What are strategies for increasing intimacy and addressing fears?

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FEMALE-ICD study (2)

N=29

> **How has your experience with your device affected the way you think and feel about your body?**

Table III.

Mean (Standard Deviation) Scores on Psychological Measures at Baseline and Posttreatment

	Intervention	Control	P-Value
FSAS			
(baseline)	22.79 (10.76)	19.73 (8.65)	0.026*
(posttreatment)	17.93 (6.02)	19.13 (7.85)	
FPAS	69.52 (16.30)	70.89 (19.76)	0.023*
	78.93 (17.03)	71.11 (19.33)	

FSAS = shock anxiety; FPAS = device acceptance.
*P-value statistic for time by group interaction effects.

Vazquez et al. PACE 2010

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Gender disparities and patient reported outcomes: Systematic review

- **18 studies; sample size ≥ 100 (range 100-645)**

- **10/18 studies were cross-sectional**

- **Focusing on anxiety, depression and quality of life**

- **No effect of gender on PROs in 80% (26/32) of the outcomes**

Inconclusive

Brouwers, van den Broek, Denollet & Pedersen. PACE 2011;34:798-803

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Gender disparities - anxiety and quality of life

N = 718

Table 2 Influence of gender on anxiety and quality of life (multivariate analysis of covariance for repeated measures)

| | PF | SF | RP | RE | MH | VT | BP | GH | Anxiety |
	F	F	F	F	F	F	F	F	F
Time	3.07	1.03	5.14§	4.66§	11.36§	0.64	2.61	2.75	2.42
Gender	7.14§	0.73	1.50	0.88	0.25	4.88§	2.65	0.20	2.67
Age	1.46	8.12§	2.32	7.74§	3.10	8.39§	1.10	14.12$^{||}$	7.85§
Marital status (yes)	0.12	0.11	0.15	1.58	0.00	1.64	0.86	0.60	0.00
Smoking	3.44	3.45	2.28	3.30	3.31	7.08§	2.05	4.06§	3.91§
Education (low)	10.71$^{||}$	1.92	9.82$^{#}$	17.84$^{#}$	12.67$^{||}$	13.04$^{||}$	5.31§	2.58	18.81$^{#}$
Working status (yes)	16.28$^{#}$	14.88$^{#}$	13.54$^{||}$	19.76$^{#}$	0.01	5.05§	2.84	12.69$^{||}$	10.14$^{||}$
Site of implantation	0.93	4.56§	0.38	1.41	5.08§	4.55§	0.38	0.91	1.93
Indication	0.10	0.00	0.01	0.00	0.11	0.53	0.20	0.38	0.46
CAD[a]	1.36	0.66	2.01	0.43	0.38	0.06	3.06	5.14§	0.23
CRT[b]	10.80$^{||}$	0.35	11.06$^{||}$	2.89	4.15§	14.82$^{#}$	0.01	11.99$^{||}$	1.46
Shocks[c]	0.08	0.88	1.35	0.65	0.15	0.09	0.02	0.97	2.47
Diabetes	17.23$^{#}$	9.86§	10.14§	9.72§	0.93	11.77§	6.79	14.97$^{||}$	5.17§
Type D personality	10.70$^{||}$	33.72$^{#}$	15.67$^{#}$	34.08$^{#}$	122.96$^{#}$	35.76$^{#}$	9.07$^{||}$	45.16$^{#}$	152.47$^{#}$
Psychotropics	13.70$^{#}$	22.49$^{#}$	12.08§	8.98§	38.02$^{#}$	21.77$^{#}$	27.59$^{#}$	12.55§	26.23$^{#}$
ACE-inhibitors	0.08	1.79	0.32	0.44	4.34§	0.28	3.13	0.14	0.19
Amiodarone	1.99	2.32	0.06	0.05	0.20	0.97	0.45	0.89	1.22
Beta-blockers	0.26	0.08	2.76	0.27	0.41	0.07	0.17	4.32§	0.23
Digoxin	0.30	1.80	0.15	0.00	0.58	0.58	1.48	2.61	2.30
Diuretics	22.38$^{#}$	10.70$^{||}$	11.55$^{||}$	1.75	0.23	9.57$^{||}$	4.30§	10.94$^{||}$	1.13
Statins	0.12	1.80	0.19	1.30	0.00	0.00	0.36	0.70	0.17

PF, Physical Functioning; SF, Social Functioning; RP, Role Physical Functioning; RE, Role Emotional Functioning; MH, Mental Health; VT, Vitality; BP, Bodily Pain; GH, General Health.
[a]Coronary artery disease.
[b]Cardiac resynchronization therapy.
[c]Both appropriate and inappropriate shocks received between implantation and 12 months follow-up.
$^{§}P < 0.05$; $^{||}P < 0.01$; $^{#}P < 0.001$.

Habibovic et al. Europace 2011

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Table 2. Medical Outcomes Survey (MOS) mean scores on discharge from hospital and at 4, 8 and 12 months

	Hospital discharge		4 months		8 months		12 months	
	Men n=33	Women n=14	Men n=33	Women n=14	Men n=33	Women n=14	Men n=33	Women n=14
MOS total	101.51 SD 21.71	105.48 SD 23.84	113.05 SD 23.44	118.15 SD 22.40	113.38 SD 20.06	119.24 SD 24.85	112.81 SD 20.33	117.83 SD 26.09
Role physical	9.60 SD 5.16	11.57 SD 5.33	12.03 SD 4.56	14.07 SD 3.79	12.15 SD 3.89	15.07[a] SD 3.89	12.48 SD 3.98	15.00 SD 4.22
Mental health	19.36 SD 3.13	16.78[a] SD 3.94	21.12 SD 3.49	20.50 SD 3.74	20.82 SD 3.00	19.86 SD 4.69	20.94 SD 2.97	19.57 SD 3.57

[a] $p < 0.05$ when comparing scores between men and women.

Table 3. State and Trait Anxiety Inventory mean scores on discharge from hospital and at 4, 8 and 12 months

Mean	Hospital discharge		4 months		8 months		12 months	
	Men n=33	Women n=14	Men n=33	Women n=14	Men n=33	Women n=14	Men n=33	Women n=14
STAI 1	35.82 SD 10.60	43.36[a] SD 12.57	34.64 SD 12.51	34.36 SD 10.77	35.03 SD 11.66	33.21 SD 12.87	32.79 SD 10.44	32.57 SD 11.57
STAI 2	33.79 SD 8.24	39.28 SD 9.96	34.15 SD 10.91	35.71 SD 10.64	34.73 SD 10.09	36.64 SD 13.83	34.82 SD 11.61	35.00 SD 13.47

STAI 1: State and Trait Anxiety Inventory.
STAI 2: State and Trait Anxiety Inventory.
[a] $p < 0.05$ when comparing scores between men and women.

Marshall et al., Cardiovas Nurs 2012

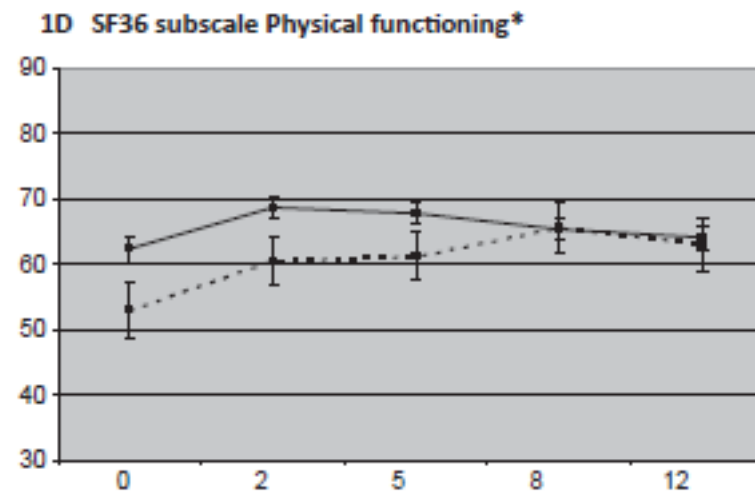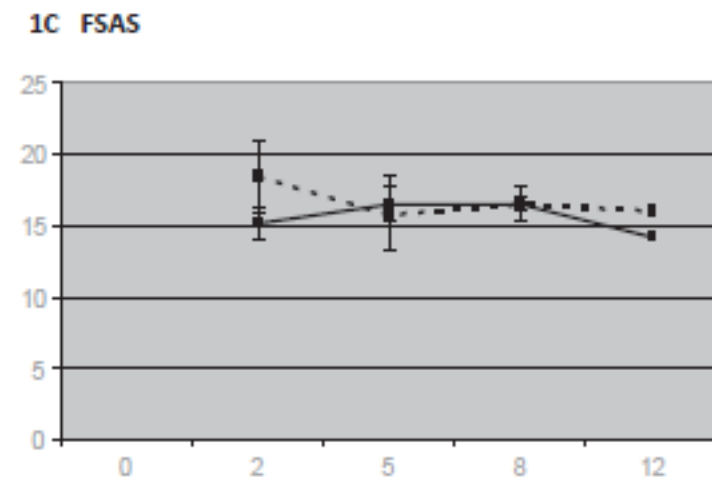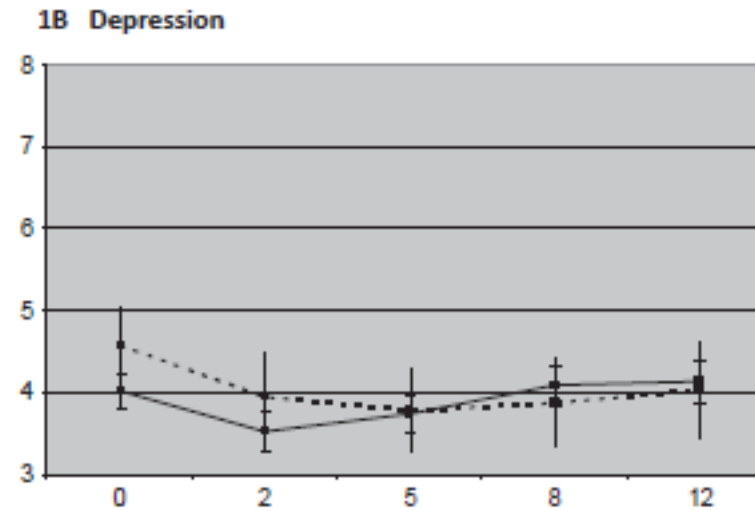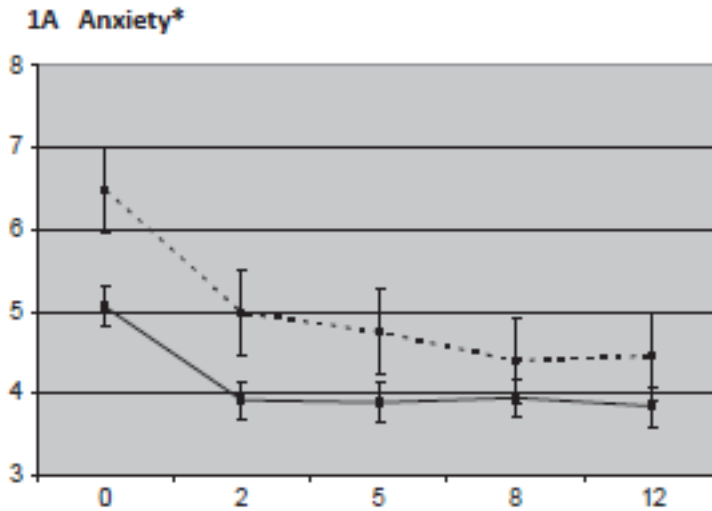**N=179**
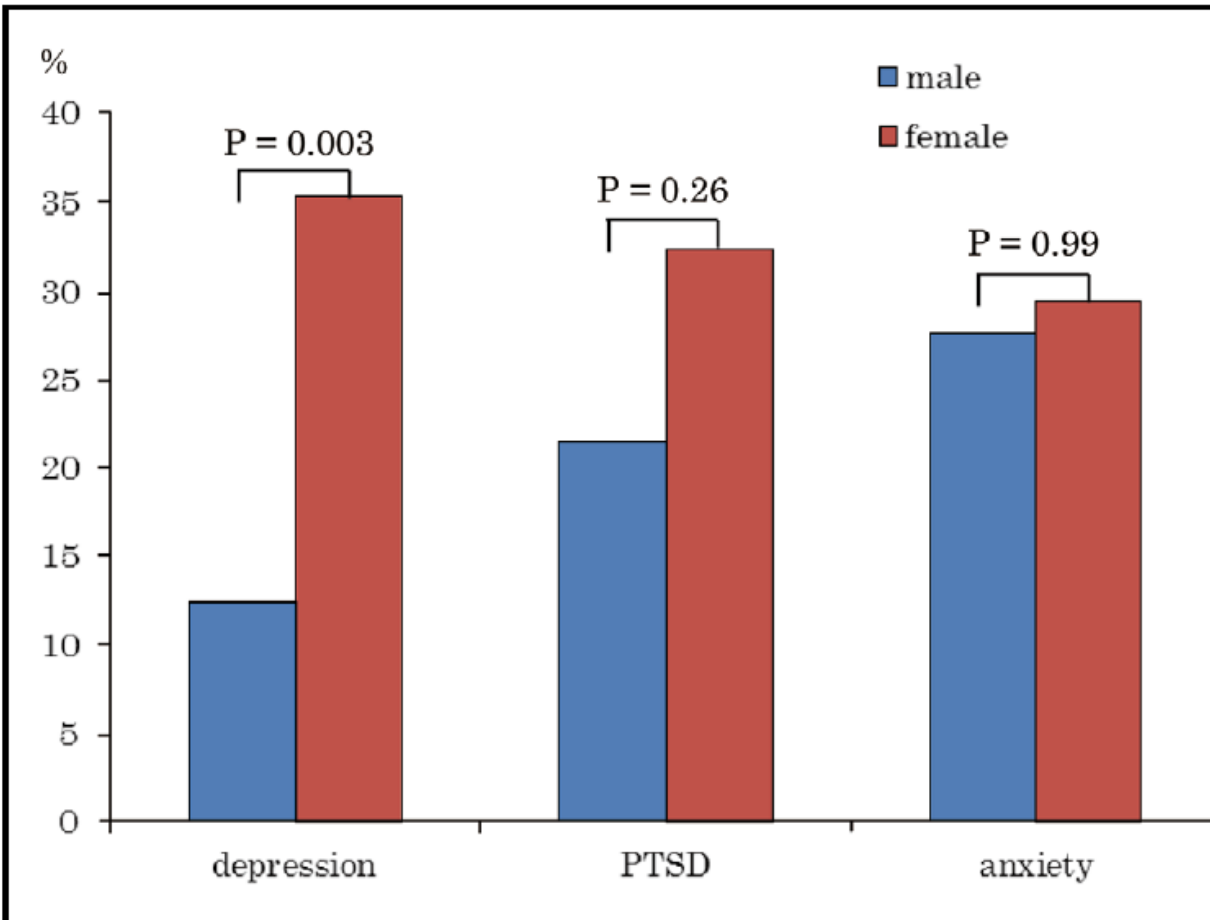
Figure. Prevalence of psychological disorders vs. gender. Presence of psychological disorders was determined using the questionnaire cut-offs. P<0.05 was considered significant. PTSD, post-traumatic stress disorder.
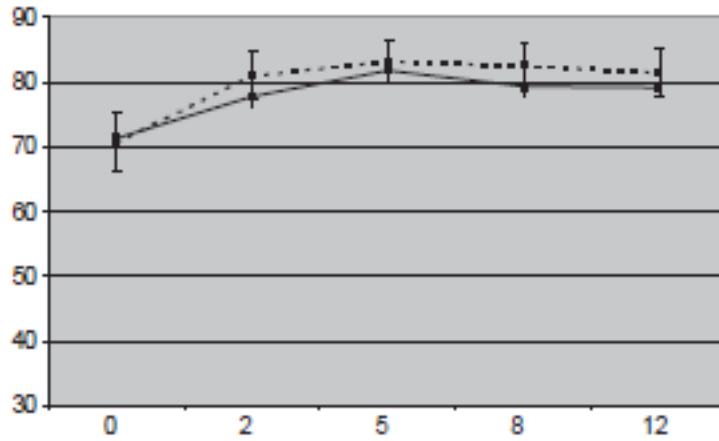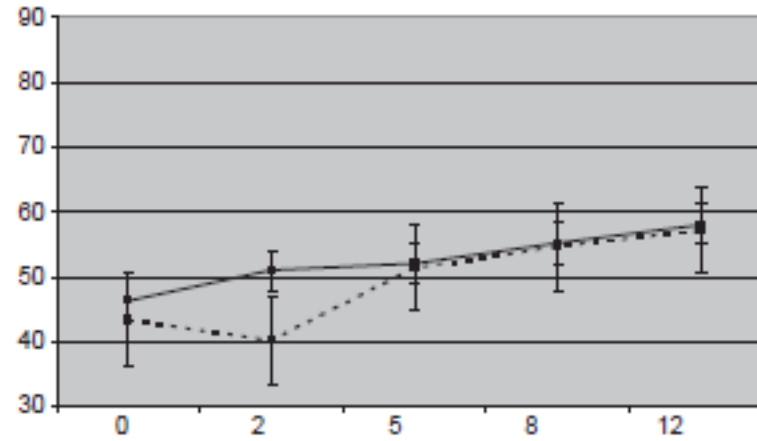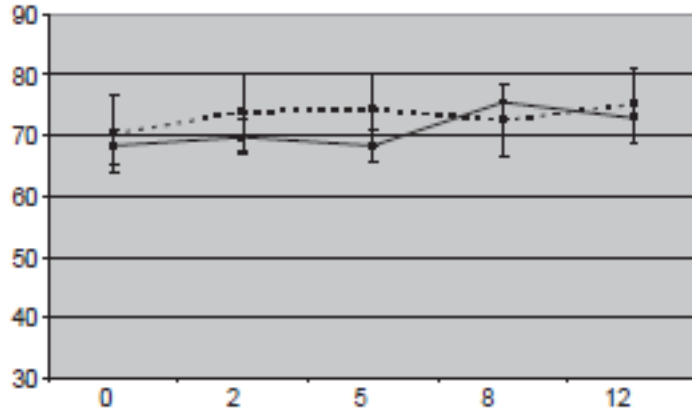
Gender disparities – well-being

N=300

1A Anxiety*

1B Depression
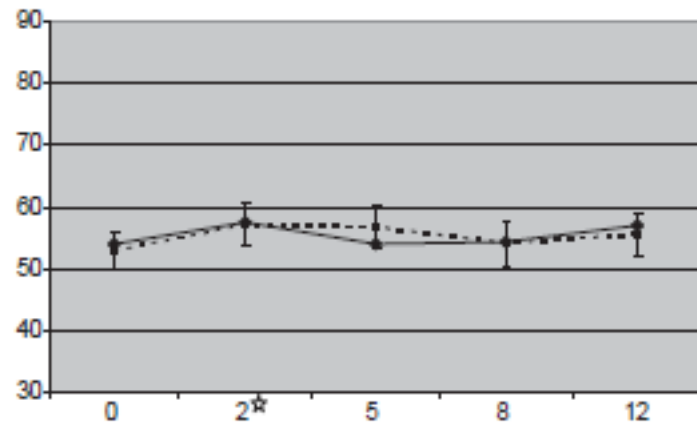
1C FSAS

1D SF36 subscale Physical functioning*

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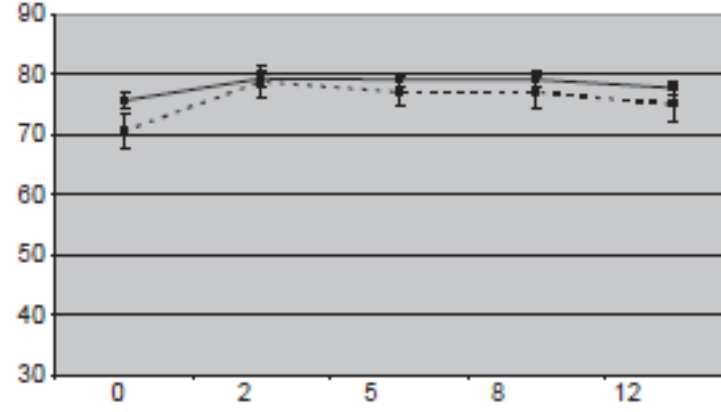
1I SF36 subscale Vitality*
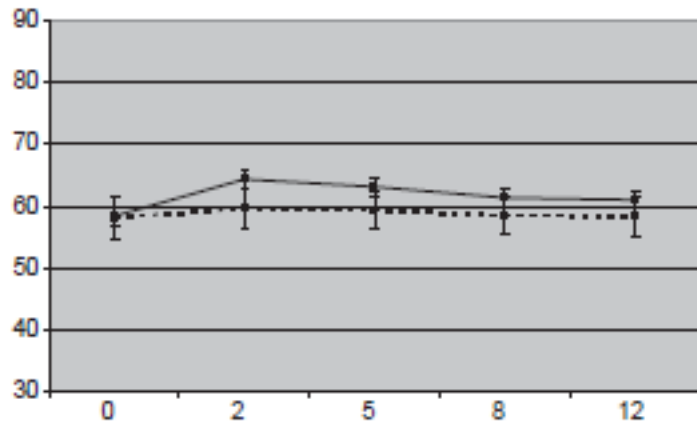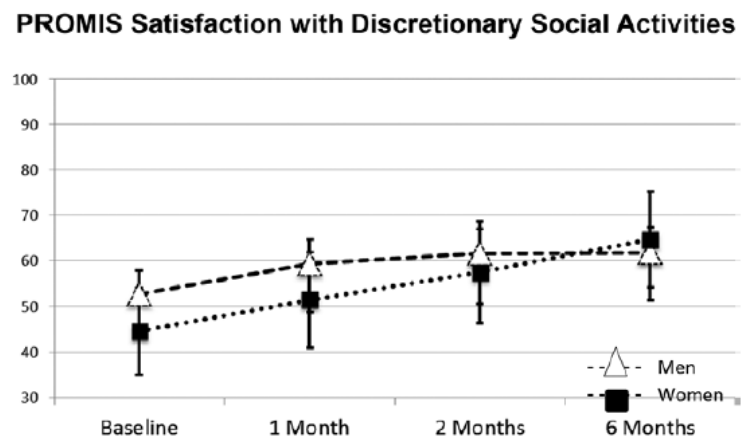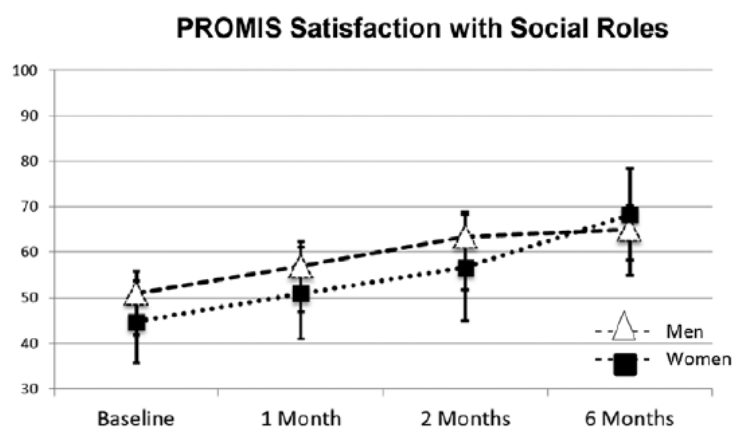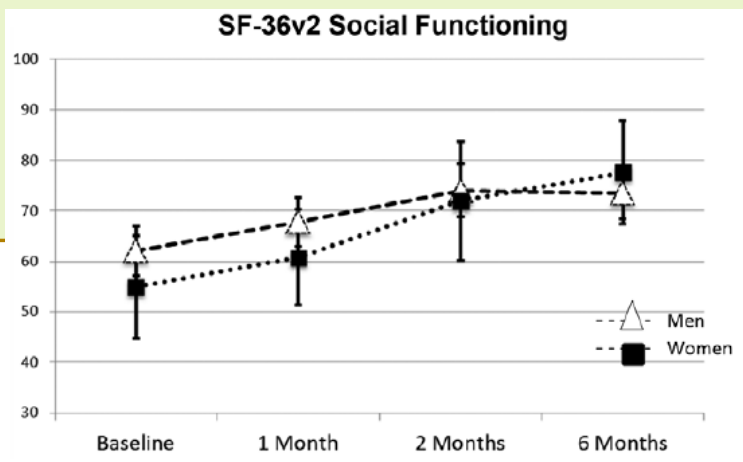
1J SF36 subscale Pain
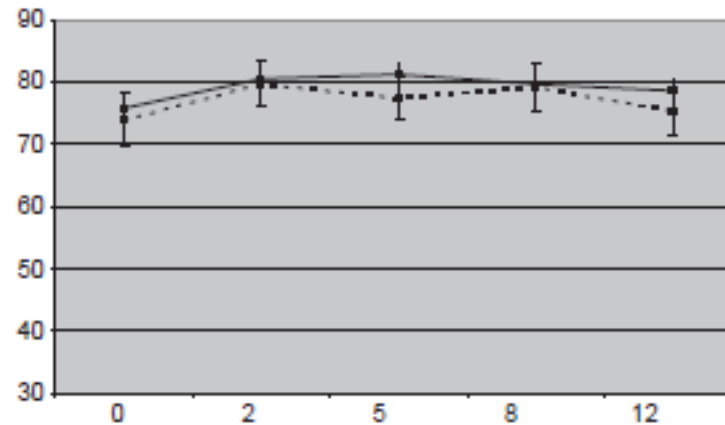
1K SF36 subscale General functioning*

Figure 2. Sex-based trajectories of temporal change in social health (mean scores and 95% confidence intervals).

WHAT IS KNOWN

- The implantable cardioverter defibrillator can be associated with changes in quality of life. Significant emphasis has been placed on the study of changes in mental health, especially anxiety and depression associated with implantable cardioverter defibrillator shocks.
- Social health is an important dimension of quality of life.

WHAT THE STUDY ADDS

- We found that social health improves in the first 6 months after implantable cardioverter defibrillator but men and women differ in their trajectory of change. Men's mean scores were higher than women's before implantation, but women improved at a faster rate in the first 6 months.
- Individual growth modeling provides novel analytic tools to study between- and within-group variation in change parameters and can inform clinical practice.

Lauck et al., Circ Cardiovasc Qual Outcomes 2015
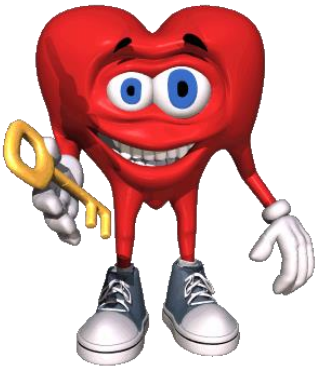
- **Few ICD studies** designed a ~~~~~~ examine gender differences in ~~~~~~ **~~~~ions** and **clinical outcome~~~~~~**

- **Available** ~~~~~~ **post hoc analyses**

- **~~~~~~** ~~~ have used **smaller sample** ~~~~ power), are **cross-sectional**, lack o~~ ~~~~priate **statistical adjustment**

Warranting new, well designed studies

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Utilization of implantable cardioverter DEFIBrillator therapy in the treatment of heart disease: Clinical and psychological outcomes in WOMEN (DEFIB-WOMEN)

CoRPS

Danish Heart Foundation

(grant 09-10-R75-A2713-22565)

Odense University Hospital (co-ordinating study center):

- **Susanne S. Pedersen** *(CoRPS, Tilburg University; Erasmus Medical Center - NL)*

- **Mogens Lytken Larsen**

- **Jens Brock Johansen**

Aarhus University Hospital (Skejby):

- **Jens Cosedis Nielsen**

Aarhus University Hospital (Aalborg):

- **Sam Riahi**

Copenhagen University Hospital (Rigshospitalet):

- **Regitze Videbæk**

Gentofte Hospital:

- **Michael Vinter Højgaard**

Study objectives - substudy 1

PATIENT REPORTED OUTCOMES:

- **Do <u>women and men</u> experience differences in distress and quality of life (including body image concerns)?**

- **Does <u>ICD indication</u> have a differential impact on quality of life in women versus men?**

- **Do <u>complications</u> have a differential influence on levels of distress and quality of life in women versus men?**

- **Do <u>shocks</u> have a differential effect on patient-reported outcomes in women versus men?**

Study objectives - substudy 2

PROCEDURE- AND DEVICE-RELATED COMPLICATIONS:

- **Do women experience more <u>procedure-related</u> <u>complications</u> than men?**

- **Is there a difference in the occurrence and reason for <u>inappropriate shocks</u> in woman as compared with men?**

Study objectives - substudy 3

MORBIDITY AND MORTALITY:

- **Are there gender differences in a composite endpoint of time to <u>onset of ventricular tachycardia's</u> and <u>mortality</u>?**

- **Do psychological factors exert a differential effect on a composite endpoint of time to <u>onset of ventricular tachycardia's</u> and <u>mortality</u> in women versus men?**

Study design

- **National, Danish, multi-center, prospective, observational study**

- **Psychological/quality of life assessments will take place at 5 time points:**

  - **T0 (baseline)**
  - **T1 (3 months post implantation)**
  - **T2 (6 months post implantation)**
  - **T3 (12 months post implantation)**
  - **T4 (24 months post implantation)**

- **Patients will also be followed up for time to ventricular tachycardia and mortality both short- and long-term (up to a period of 10 years)**

Participants

- **N = 1656; 546 (33%) women**

- **Inclusion period = 2 years**

- **2068 patients being implanted with an ICD in the five centers during a period of 2 years, and an expected response rate of 80%**

Inclusion and exclusion criteria

Inclusion criteria:

- First-time ICD implantation
- 18-80 years of age
- Male or female
- Speaking and understanding Danish
- Providing written informed consent
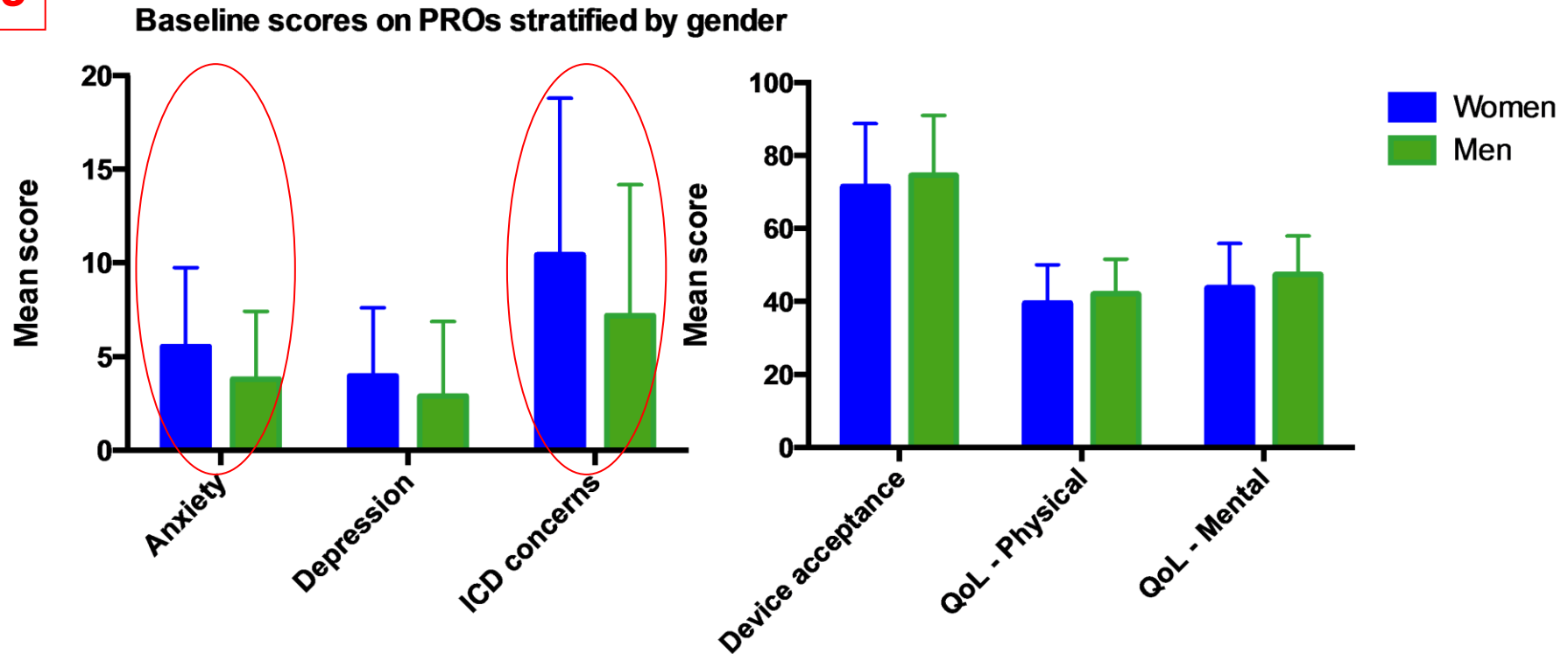
Exclusion criteria:

- Life expectancy <1 year
- History of psychiatric illness other than affective/anxiety disorders
- On the waiting list for heart transplantation
- Insufficient knowledge of the Danish language

Baseline

Women

-Younger

-Less likely to be married

-Less likely to be employed

-More likely to receive psychological treatment

-Higher educated

Baseline scores on PROs stratified by gender

Preliminary findings

N=1766

Pedersen SS et al., 2015 unpublished data

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Conclusions

- **Findings to date are inconclusive but show a trend towards decreased functioning in women in particular domains**
- **Large, sufficiently powered trials are needed**
- **Too soon for interventions**

- *DEFIB-WOMEN*